Taste assessment of electrospun chlorpheniramine maleate fibres using an electronic taste sensing system

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Introduction

Bitter tasting medicines present a compliance barrier to the paediatric population. Innovative techniques, such as electrospinning, have the potential to mask the drug bitterness whilst manufacturing an easy to swallow formulation. In this study chlorpheniramine maleate (CPM) was electrospun with the taste masking polymer Eudragit E-EPO (E-EPO). The taste masking efficiency of the manufactured fibres were assessed using an electronic tasting system (E-tongue).

Aim

- The primary aim of this study was to ascertain the detectability of the bitter taste of CPM by the e-tongue.
- The secondary aim was to evaluate the taste masking effectiveness of electrospun CPM fibres.

Materials and Methods

Materials: E-EPO was donated by Evonik (Darmstadt, Germany). CPM was purchased from Cambridge Bioscience (Cambridge, UK).

Electrospinning: Solutions of E-EPO were prepared in absolute ethanol. Spraybase® (Cambridge, USA) electrospinning apparatus was used to manufacture fibres with 1:6, 1:7, and 1:8 drug to polymer ratios.

Taste assessment: TS-5000Z (Insent Inc., Atsugi-shi, Japan) electronic tongue was used to assess the taste of the samples.

- Pure CPM was tested at 5 different concentrations using the clinical dose as a guide (0.25, 0.5, 1, 2 and 4 mg/mL) .
- Pure E-EPO, physical mixtures, placebo fibres, and CPM fibres were all tested by dissolving the equivalent of 20 paediatric doses (20mg) in 100mL of 10mmol KCl solution, used as a supporting electrolyte. The mixture was then stirred for 1 minute at 37°C before being filtered out and tested.

Data analysis: All experiments were run in triplicate and Euclidean distances were calculated from cluster centres. OriginPro (Massachusetts, USA) 2017 was used to complete a multivariate principal component analysis (PCA).

Results and Discussion

CPM's taste was found to be detectable by the E-tongue sensors, as a basic bitter tastant. **Figure 1** shows a concentration dependent response to CPM.

PCA: Out of the four sensors, the basic bitterness receptor AC0, had an eigenvalue of 3.8, equating to 95% of variance, and therefore was responsible for principal component 1. AN0, the second basic bitterness receptor , was responsible for principle component 2.

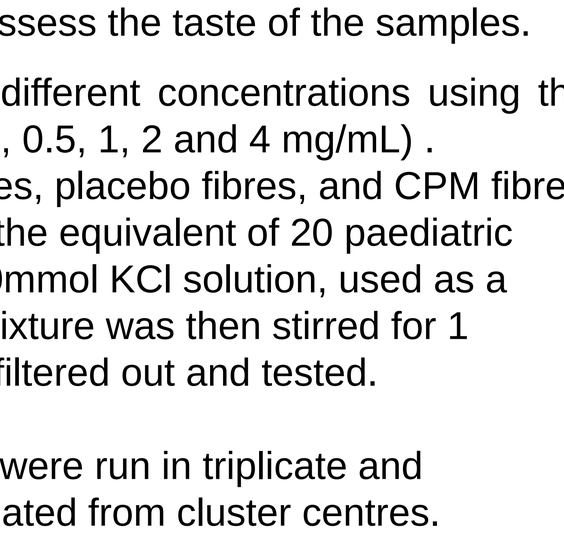

Figure 1 – Analysis of sensor responses to various concentrations of CPM: AC0 – basic bitterness; AN0 – basic bitterness; C00 - acidic bitterness; AE1 – astringency.

Euclidean distances were calculated to determine the differences between the pure drug, physical mixtures, placebo and drug loaded fibre. These values are shown in **Table 1.**

Table 1 – Euclidean distances from drug loaded fibres, placebo fibres, physical mixtures, pure E-EPO, to pure CPM.

Sample	Equivalent Amount (mg)		Euclidean distance
	E-EPO	CPM	
Physical Mixture 1:6	120	20	4.1
Physical Mixture 1:7	140	20	5.1
Physical Mixture 1:8	160	20	5.4
Active fibre 1:6 30% E-EPO	120	20	7.4
Active fibre 1:6 40% E-EPO	120	20	7.5
Active fibre 1:6 35% E-EPO	120	20	7.9
Active fibre 1:8 35% E-EPO	160	20	9.0
Active fibre 1:7 35% E-EPO	140	20	9.2
Placebo fibre 1:6, 30% E-EPO	120	0	21.8
Pure E-EPO 1:8	800	0	22.1
Pure E-EPO 1:6	600	0	22.8
Pure E-EPO 1:7	700	0	24.0

The greater the Euclidean distance between the pure drug and the formulation, the greater the difference in taste, and hence the best taste masking effect. **Figure 2** shows a map adapted from the sensor responses for all the samples tested. As anticipated, pure E-EPO had the largest Euclidean distance from pure CPM. Drug loaded fibres had a larger distance than the physical mixture, indicating better taste masking. However, drug loaded fibres Euclidean distances' were closer to the physical mixtures than the placebo fibre, which may indicate some drug release.

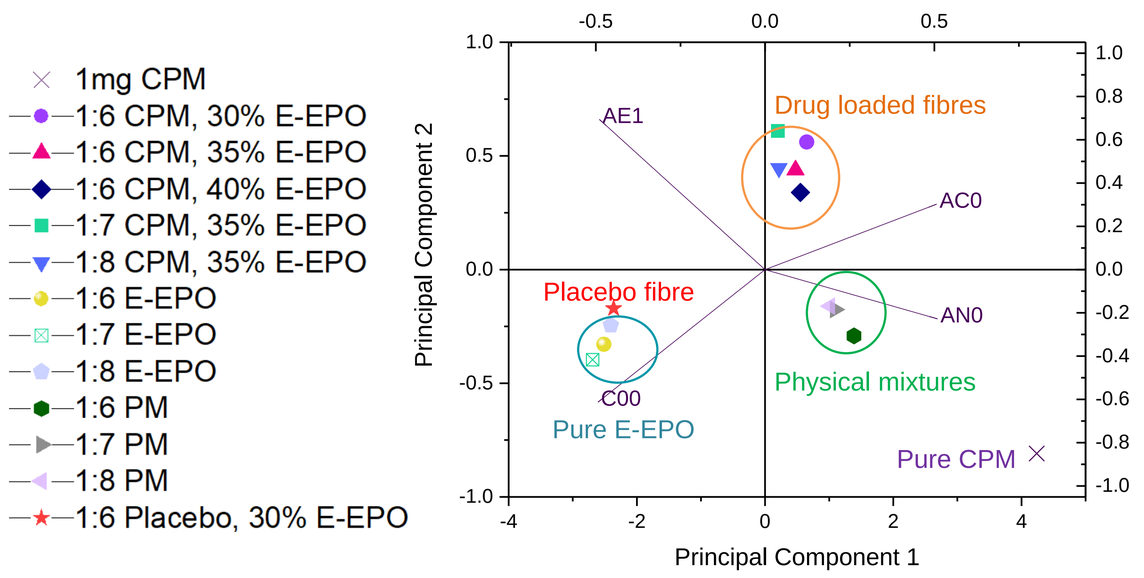

Figure 2 – PCA biplot of drug loaded fibres compared to their physical mixtures, placebo fibre, pure E-EPO and pure CPM.

Conclusions

The E-tongue is an appropriate method to test the taste of CPM and therefore CPM formulations. This is the first study to look at taste assessment of electrospun CPM with E-EPO. There is some indication that taste masking may be improved by electrospinning the drug with E-EPO, compared to the physical mixture.

Future work: Further dissolution studies can quantity the exact amount of drug release. Results obtained from the E-tongue can be further verified using a human taste panel or using an animal model.

Acknowledgments

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